

SHEET 1 OF 4

SUBSTITUTE FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE

ATTY. DOCKET NO.  
02-40052-US-PSERIAL NO.  
10/725,064

## INFORMATION DISCLOSURE CITATION

APPLICANT:  
SummarFILING DATE  
December 1, 2003GROUP  
TBD

## U.S. PATENT DOCUMENTS

| DISPATENT DOCUMENTS |           |                 |            |                 |       |          |                                 |
|---------------------|-----------|-----------------|------------|-----------------|-------|----------|---------------------------------|
| EXAMINER<br>INITIAL |           | DOCUMENT NUMBER | DATE       | NAME            | CLASS | SUBCLASS | FILING DATE (IF<br>APPROPRIATE) |
| AL                  | AA        | 4,284,647       | 08/18/1981 | Brusilow et al. |       |          |                                 |
|                     | AB        | 4,457,942       | 07/03/1984 | Brusilow        |       |          |                                 |
|                     | AC        | 5,605,930       | 02/25/1997 | Samid           |       |          |                                 |
|                     | AD        | 5,635,532       | 06/03/1997 | Samid           |       |          |                                 |
|                     | AE        | 5,635,533       | 06/03/1997 | Samid           |       |          |                                 |
|                     | AF        | 5,654,333       | 08/05/1997 | Samid           |       |          |                                 |
|                     | AG        | 5,661,179       | 08/26/1997 | Samid           |       |          |                                 |
|                     | AH        | 5,708,025       | 01/13/1998 | Samid           |       |          |                                 |
|                     | AI        | 5,710,178       | 01/20/1998 | Samid           |       |          |                                 |
|                     | AJ        | 5,712,307       | 01/27/1998 | Samid           |       |          |                                 |
|                     | AK        | 5,843,994       | 12/01/1998 | Samid           |       |          |                                 |
|                     | AL        | 5,852,056       | 12/22/1998 | Samid           |       |          |                                 |
|                     | AM        | 5,877,213       | 03/02/1999 | Samid           |       |          |                                 |
|                     | AN        | 5,883,124       | 03/16/1999 | Samid           |       |          |                                 |
|                     | AO        | 5,968,979       | 10/19/1999 | Brusilow        |       |          |                                 |
|                     | AP        | 6,037,376       | 03/14/2000 | Samid           |       |          |                                 |
|                     | AQ        | 6,060,510       | 05/09/2000 | Brusilow        |       |          |                                 |
| AR                  | 6,083,984 | 07/04/2000      | Brusilow   |                 |       |          |                                 |

## FOREIGN PATENT DOCUMENTS

|  |  | DOCUMENT NO. | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION<br>YES | TRANSLATION<br>NO |
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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|  |    |                                                                                                                                                 |
|--|----|-------------------------------------------------------------------------------------------------------------------------------------------------|
|  | BA | Albrecht et al., "Hepatic Encephalopathy: Molecular Mechanisms Underlying the Clinical Syndrome," J. Neurol. Sci. 1999 Nov. 30; 170(2): 138-46. |
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SHEET 2 OF 4

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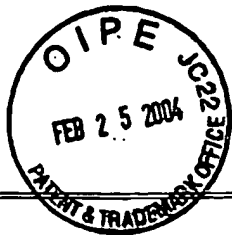
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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |                                                                                                                                                                                                  |
|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| BB | Albrecht, "Roles of Neuroactive Amino Acids in Ammonia Neurotoxicity," J. Neurosci. Res. 1998 Jan. 15; 51(2): 133-8.                                                                             |
| BC | Applegarth et al., "Incidence of Inborn Errors of Metabolism in British Columbia," 1969-1996, Pediatrics 2000 Jan.; 105(1): e10.                                                                 |
| BD | Batshaw, "Inborn Errors of Urea Synthesis," Ann. Neurol. 1994 Feb.; 35(2): 133-41.                                                                                                               |
| BE | Batshaw, "Hyperammonemia," Curr. Probl. Pediatr., 1984 Nov.; 14(11): 1-69.                                                                                                                       |
| BF | Becker et al., "Metabolic Disease," Textbook of Neuropathology, Baltimore: Williams & Wilkins, 1997; 487.                                                                                        |
| BG | Brenningstall, "Neurologic Syndromes in Hyperammonemic Disorders," Pediatr. Neurol. 1986 Sept.-Oct.; 2(5): 253-62.                                                                               |
| BH | Brusilow et al., "Urea Cycle Disorders," The Metabolic and Molecular Bases of Inherited Disease, New York: McGraw-Hill, 1995; 1: 1187-1232.                                                      |
| BI | Collins et al., "Neonatal Argininosuccinic Aciduria-Survival After Early Diagnosis and Dietary Management," J. Pediatr. 1980 Mar.; 96 (3 Pt. 1): 429-31.                                         |
| BJ | Del Rosario et al., "Hyperammonemic Encephalopathy After Chemotherapy. Survival After Treatment with Sodium Benzoate and Sodium Phenylacetate," J. Clin. Gastroenterol. 1997 Dec.; 25(4): 682-4. |
| BK | Feillet et al., "Alternative Pathway Therapy for Urea Cycle Disorders," J. Inherit. Metab. Dis. 1998; 21 Suppl 1: 101-111.                                                                       |
| BL | Felipo et al., "Molecular Mechanism of Acute Ammonia Toxicity and of its Prevention by L-Carnitine," Adv. Exp. Med. Biol. 1994; 368: 65-77.                                                      |
| BM | Hauser et al., "Allopurinol-Induced Orotidinuria. A Test for Mutations at the Ornithine Carbamoyltransferase Locus in Women," N. Engl. J. Med., 1990 Jun. 7; 322(23): 1641-5.                    |
| BN | Kuntze et al., "Hyperammonemic Coma Due to Proteus Infection," J. Urol. 1985 Nov.; 134(5): 972-3.                                                                                                |
| BO | Logan, "Neonatal Hyperammonemic Encephalopathy. Topics in Neonatal Neurology," Orlando: Grune & Stratton 1984; 137-157.                                                                          |
| BP | Maestri et al., "Plasma Glutamine Concentration: A Guide in the Management of Urea Cycle Disorders," J. Pediatr. 1992 Aug.; 121(2): 259-61.                                                      |

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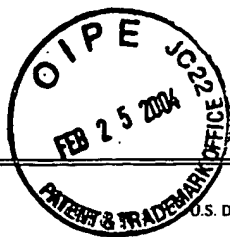
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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |    |                                                                                                                                                                                                                                                                                                                                                 |
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| al | BQ | Msall et al., "Neurologic Outcome in Children with Inborn Errors of Urea Synthesis. Outcome of Urea-Cycle Enzymopathies," N. Engl. J. Med., 1984 Jun. 7; 310(23): 1500-5.                                                                                                                                                                       |
|    | BR | Prasad et al., "Argininemia: A Treatable Genetic Cause of Progressive Spastic Diplegia Simulating Cerebral Palsy: Case Reports and Literature Review," J. Child. Neurol. 1997 Aug.; 12(5): 301-9.                                                                                                                                               |
|    | BS | Ratnaike et al., Hyperammonaemia and Hepatotoxicity During Chronic Valproate Therapy: Enhancement by Combination with Other Antiepileptic Drugs," Br. J. Clin. Pharmacol. 1986 Jul.; 22(1): 100-3.                                                                                                                                              |
|    | BT | Schaefer et al., "Dialysis in Neonates with Inborn Errors of Metabolism," Nephrol. Dial. Transplant, 1999 Apr.; 14(4): 910-8.                                                                                                                                                                                                                   |
|    | BU | Schutze et al., "Hyperammonemia and Neonatal Herpes Simplex Pneumonitis," Pediatr. Infect. Dis. J., 1990 Oct.; 9(10): 749-50.                                                                                                                                                                                                                   |
|    | BV | Uchino et al., "Neurodevelopmental Outcome of Long-term Therapy of Urea Cycle Disorders in Japan," J. Inherit. Metab. Dis. 21 1998; 21 Suppl 1: 151-9.                                                                                                                                                                                          |
|    | BW | Whittington et al., "Liver Transplantation for the Treatment of Urea Cycle Disorders," J. Inherit Metab. Dis., 1998; 21 Suppl 1: 112-8.                                                                                                                                                                                                         |
|    | BX | Williams et al., "Valproic Acid-Induced Hyperammonemia in Mentally Retarded Adults," Neurology 1984 Apr.; 34(4): 550-3.                                                                                                                                                                                                                         |
|    | BY | Petersdorf, et al., Harrison's Principles of Internal Medicine, 10 <sup>th</sup> Edition, McGraw-Hill 1983; 125, 1775, 1781, 1814-16, 2108-09.                                                                                                                                                                                                  |
|    | BZ | Beers et al., The Merck Manual of Diagnosis and Therapy, Seventeenth Edition, Merck Research Laboratories, 1999, 362-5, 372-6.                                                                                                                                                                                                                  |
|    | CA | The Merck Manual, Sec. 4, Ch. 38, Clinical Features of Liver Disease, Portal-Systemic Encephalopathy, available at <a href="http://www.merck.com/pubs/mmanual/section4/chapter38/38f.htm">http://www.merck.com/pubs/mmanual/section4/chapter38/38f.htm</a> , 6/23/2003.                                                                         |
|    | CB | What is a Urea Cycle Disorder?, available at <a href="http://www.nucdf.org/whatis.htm">http://www.nucdf.org/whatis.htm</a> , 9/25/2003.                                                                                                                                                                                                         |
|    | CC | Hepatic Encephalopathy, available at <a href="http://members.tripod.com/enotes/hepatic-encephalopathy.htm">http://members.tripod.com/enotes/hepatic-encephalopathy.htm</a> , 6/24/2003.                                                                                                                                                         |
|    | CD | Excerpt from Portal-Systemic Encephalopathy, available at <a href="http://www.emedicine.com/med/byname/portal-system-encephalopathy.htm">http://www.emedicine.com/med/byname/portal-system-encephalopathy.htm</a> , 6/24/2003.                                                                                                                  |
|    | CE | Watanabe, Portal-Systemic Encephalopathy in Non-Cirrhotic Patients: Classification of Clinical Types, Diagnosis and Treatment Journal of Gastroenterology and Hepatology 15(9): 969-79, available at <a href="http://archive.mail-list.com/hbv_research/msg01824.html">http://archive.mail-list.com/hbv_research/msg01824.html</a> , 6/24/2003. |

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|    |    |                                                                                                                                                                                                                                                  |
|----|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| al | CG | Butterworth, "Effects of Hyperammonaemia on Brain Function," J. Inher. Metab. Dis. 21 (Suppl 1) 1998; 6-20.                                                                                                                                      |
|    | CH | Lee et al., "In vivo urea cycle flux distinguishes and correlates with phenotypic severity in disorders of the urea cycle," PNAS 2000 July 5; 97(14): 8021-8026.                                                                                 |
|    | CI | Way, "Portal Hypertension," Current Surgical Diagnosis & Treatment, 10 <sup>th</sup> edition, Appleton & Lange; 1994: 520-536.                                                                                                                   |
|    | CJ | Ferenci et al., "Hepatic Encephalopathy-Definition, Nomenclature, Diagnosis, and Quantification: Final Report of the Working Party at the 11 <sup>th</sup> World Congresses of Gastroenterology, Vienna, 1998", Hepatology 2002; 35(3): 716-721. |
|    | CK | Sanyal et al., "Portosystemic Encephalopathy After Transjugular Intrahepatic Portosystemic Shunt: Results of a Prospective Controlled Study," Hepatology 1994; 20(1 Pt. 1): 46-45.                                                               |
|    | CL | Riggio et al., "Hepatic Encephalopathy After Transjugular Intrahepatic Portosystemic Shunt. Incidence and Risk Factors," Digestive Diseases and Sciences, 1996 March; 41(3): 578-584.                                                            |
|    | CM | Thuluvath et al., "TIPS for Management of Refractory Ascites. Response and Survival Are Both Unpredictable," Digestive Diseases and Science 2003 March; 48(3): 542-550.                                                                          |
|    | CN | Groeneweg et al., "Subclinical Hepatic Encephalopathy Impairs Daily Functioning," Hepatology 1998 July; 28(1): 45-49.                                                                                                                            |

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